3. THE USP CLASSIFICATION SYSTEM

Background: How Does the USP Classification System Work?

Under the MMA, plans can establish their own formularies, as long as they do not use this flexibility to design formularies that would discourage high-cost beneficiaries from enrolling. Within each therapeutic category in the plan's system, at least two drugs must be on the formulary. Thus, for example, if Cox-II inhibitors (e.g., Celebrex) are grouped in the same class as other nonsteroidal anti-inflammatory drugs (NSAIDs) for relief of pain in a plan's formulary, then the plan can exclude these costly drugs from its formulary by including two NSAIDs that are not Cox-II inhibitors. However, if the Cox-II drugs are their own class, at least two must be on the formulary. CMS has moved beyond this basic rule in establishing regulatory guidelines, as described below.

The MMA required that United States Pharmacopeia (USP) develop a model classification system for use in describing plan formularies. This model system, once ratified by CMS, provides plans that follow it a "safe harbor": their classification systems will be deemed not to be discouraging high-cost beneficiaries, though the actual formulary must still be reviewed. The MMA authorized USP to draw upon their private-sector experience to create a classification scheme (rather than choosing from one of the existing classification schemes) that would be universally applied to all evaluations of PDP formularies. It is not known to what extent plans will follow the final USP model. Some plans may choose to use the approved classification system because it provides them a "safe harbor" guaranteeing approval of their system. Other plans may choose to use a different system if they believe it gives them greater opportunities to achieve cost containment goals.

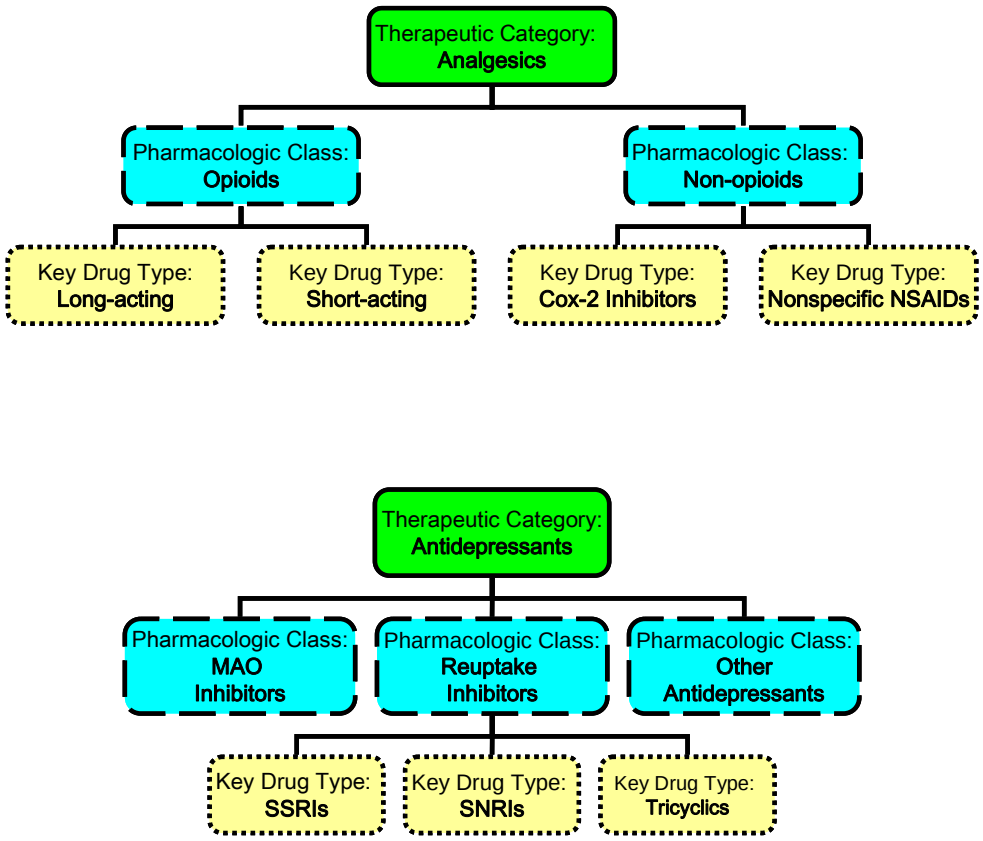
Figure 3 shows two examples of the way the USP system organizes drugs into a hierarchy. The boxes with solid lines (analgesics and antidepressants) indicate two of USP's 41 therapeutic categories. In the USP system, these therapeutic categories are typically based on diseases or symptoms that drugs are used to treat – such as pain and depression.

Most therapeutic categories are broken into pharmacologic classes (represented by the boxes with broken lines), primarily based on drugs' mechanisms of action. The combination of these classes and the therapeutic categories that are not subdivided into classes create 146 unique groupings. For each of these unique classes, CMS rules state that a plan must cover at least two drugs (where there are at least two) if it chooses to use the model guidelines as the basis of its formulary. For example, under this rule, a plan would have to cover 2 drugs in the class of MAO inhibitors.

Classes are sometimes, but not always, further subdivided into key drug types to illustrate drug groups that would further ensure beneficiary access to needed drugs. In Figure 3, the key drug types are represented by the boxes with dotted lines. Note that while both of the pharmacologic classes of analgesics are broken into key drug types, only one of the classes of antidepressants includes key drug types. The 118 key drug types in the USP scheme are not part of the official classification system. However, they are recognized through the CMS formulary guidelines: for each of these key drug types, a plan must cover at least one drug.

Thus, for example, in the class of reuptake inhibitors, a plan must cover at least one SSRI, one SNRI, and one tricyclic.

Figure 3. USP Classification System for Two Therapeutic Classes



Utilization of drugs is not distributed evenly across these classes and categories. Based on data from the 2001 Medicare Current Beneficiary Survey (MCBS), the top 10 of the 41 USP therapeutic categories contain two thirds of all utilization by Medicare beneficiaries (Figure 4). [1] In fact, the cardiovascular category alone represents nearly 30% of the overall drug volume. It should be noted that two of the larger categories (autonomic drugs and anti-inflammatories) are substantially overlapping with two other categories. Most autonomic drugs are also categorized as cardiovascular drugs, and most anti-inflammatories are also analgesics.

The distribution of drugs is uneven at the class level and key drug type level as well. Over half of drug volume falls in just 15 of the 146 unique classes (Figure 5). Some of the classes in the cardiovascular category are actually as big as most of the other categories. A quarter of the volume is in the top ten key drug types (Figure 6). Appendix D gives a further breakdown of utilization by USP class, category, and key type.

[1] As discussed below, the USP fails to list drugs that account for approximately 15 percent of utilization as reported in the 2001 MCBS. The numbers in Figures 4, 5, and 6 are shown as percentages of all MCBS volume, including utilization of drugs excluded from the USP scheme. If these excluded drugs were removed from the denominator, the percentages in these tables would be higher.

Figure 4. Top Ten USP Categories

Therapeutic Category	% 2001 MCBS Volume
Cardiovascular Agents	29.95
Hormonal Agents, Stimulant/ Replacement/Modifying	6.13
Autonomic Agents	5.87
Respiratory Tract Agents	5.68
Gastrointestinal Agents	3.64
Blood Glucose Regulators	3.37
Antidepressants	3.20
Blood Products/Modifiers/ Volume Expanders	3.12
Analgesics	2.88
Anti-Inflammatories	2.57

Figure 5. Top Ten USP Classes

Pharmacologic Class	% 2001 MCBS Volume
Renin-Angiotensin-Aldosterone System Inhibitors	5.71
Sympatholytics	5.54
Dyslipidemics	4.63
Beta-Adrenergic Blocking Agents	4.23
Diuretics	4.01
Calcium Channel Blocking Agents	3.88
Hypoglycemics, Oral	3.30
Antiarrhythmics	3.12
Reuptake Inhibitors	2.67
Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)	2.57

Figure 6. Top Ten USP Key Drug Types

Key Drug Type	% 2001 MCBS Volume
Beta-Adrenergic Blocking Agents	4.36
Angiotensin-Converting Enzyme (ACE) Inhibitors	4.26
3-Hydroxy-3-Methylglutaryl Coenzyme A (HNG COA) Reductase Inhibitors	4.16
Cardioselective Beta-Adrenergic Blocking Agents	3.38
Loop Diuretics	2.51
Anticoagulants, Oral	2.31
Dihydropyridines	2.18
Antiarrhythmics - Class IV	1.93
Estrogens	1.71
Calcium Channel Blocking Agents (Non-Dihydropyridines)	1.71

The numbers above are based on the number of prescriptions for each category, class, and key drug type. An analysis of dollar volumes yields similar, though not identical, results. For example, immunological and gastrointestinal drugs have higher dollar volume than prescription volume because some of the most commonly used drugs in these categories are expensive drugs.

Technically, the USP system does not place drugs into the classification system. Because it is difficult to understand the system without showing what drugs fall into what category, the USP has displayed a list of drugs in each category and class. Although this list does not have the official imprimatur of CMS, it has been used throughout this project. In creating this new classification system, USP made a number of decisions, such as which drugs and which forms of those drugs to include. These decisions bear policy implications that are discussed below.

Policy Implications: The USP System

How drugs are defined can have a significant impact on formulary rules and standards. Two products may be considered the same drug by one system, while they are treated as separate entities by another system. The FDA's National Drug Codes (NDC) are extremely exact, for example, and give a separate code for every possible combination of chemical ingredients, strength (e.g., number of milligrams), form, package size (how many doses are typically included in one container used by the pharmacy), and the firm that manufactures or distributes the drug. USP coding, on the other hand, is more general and lists only chemical ingredients. Considerations such as brand vs. generic, strength, and (in most cases) form are absent from the USP scheme.

What Drugs Are Included. The absence of a clear-cut definition of which drug products should be considered different entities makes it considerably more difficult to interpret the statutory requirement that two drugs be covered in a given category or class. Some of the considerations that complicate this determination include the following:

- Should oral and topical forms be counted separately, especially if they are used to treat different conditions? It appears that the answer could be different for different drugs, since some appear in separate places in the USP classification and others do not.
- Should all versions of a drug (i.e., all NDC codes) be covered if at least one is covered? In their June guidance to plans, CMS stated that they will not require all dosages to be included, or all manufacturers' versions of a multi-source product to be included. In addition, CMS' guidance on displaying plan formularies makes it clear that plans may place different strengths of a drug on different cost-sharing tiers.
- How should extended-release versions of a drug be treated? It appears that CMS will neither require plans to cover extended-release versions of drugs, nor count them as an additional drug toward the coverage requirements. However, there may be instances where the extended-release version of a drug has specific medical indications that go beyond simply being more convenient for the patient.
- Should two chemically similar, but not identical, drugs count as two drugs? In the case of Celexa and Lexapro (two chemically similar anti-depressants with rather

different treatment indications), CMS has allowed an exception to the requirement that plan formularies include all anti-depressants. The manufacturer of Lexapro and several clinical groups have raised strong objections to this decision.

Policymakers will undoubtedly continue to confront the policy implications of these apparently technical questions. For the purposes of the analysis in this project, however, we made certain assumptions that allowed us to proceed unambiguously, although differences among various databases made this a programming challenge. In this project, we attempted to follow the USP classification scheme on the inclusion of drugs. The USP list became our master list against which all other formularies were compared. The exception is that for many analyses, we maintained a distinction between brand and generic drugs, while the USP does not. We have treated all forms, strengths, and extended release versions associated with a drug name to be one drug for the purposes of simplifying our analyses.

Combination Drugs and Other Omitted Drugs. There are a number of drugs excluded from the USP system. Some types of drugs are systematically excluded, while others seem to be more random. The total volume in the MCBS of the drugs not represented in the USP classification scheme is approximately 15% of all drug volume.

Unlike any other system that we studied, USP leaves out most combination products, including many that are heavily used. At the same time, about two dozen combination drugs are included in USP's list – representing a seemingly random list that includes AIDS drugs that are essential components of treatment and some common drugs for treatment of relatively minor conditions. It is difficult to deduce a reason why some are included and others are not.

Should a combination drug be counted as one of the two drugs per class? At present, CMS has determined that it should not, but this removes some incentive for plans to include these drugs on their formulary. Since a PDP will receive no credit toward meeting CMS standards if they cover these excluded combination drugs, PDPs have a reduced incentive to cover them. Careful analysis of the prevalence of these excluded drugs and their importance in clinical practice may suggest the need for USP's classification scheme to be modified in MMA's second year to better accommodate the needs of Medicare beneficiaries.

The USP system also excludes drugs that will not be covered under Part D. These include drugs covered by Part B as well as benzodiazepines, barbiturates, drugs for weight gain and weight loss, and over the counter drugs. The focus on Part D drugs makes sense in the context for which the USP system is intended, but it may limit the usefulness of the USP system for other applications.

Finally, the USP scheme omits some single-ingredient drugs for no readily apparent reason. These may simply represent errors. However, until such omissions are corrected or justified, these drugs may be less likely to appear on plan formularies.

Drugs in Multiple Categories. Like some (but not all) systems, USP lists some drugs in more than one category. Sometimes these multiple listings appear to be for different forms of a drug. Approximately 50 drugs on the USP list treat different ailments when ingested in different forms and thus are listed in more than one category or class. For instance, doxepin

may be used as an oral medication to treat depression, or as a topical cream to relieve itching.

Other drugs (112 on the USP list) may be used to treat various ailments, but in the same form. Compazine (prochlorperazine) may be prescribed in pill form as an anti-emetic or an anti-psychotic. Again, these drugs are listed in multiple categories or classes corresponding to these different uses.

Some drugs can be administered in different forms, but treat the same ailment regardless of which form is used. For example, Diclofenac is listed in four places in the USP scheme: analgesics, anti-inflammatories, dermatological agents, and ophthalmic agents.

PDP formularies may not necessarily mirror USP's classification of these drugs. About half of all the formularies we studied classify drugs in multiple classes because they have multiple uses, while the remaining formularies force each individual drug into only one class. In most cases, a covered drug will be covered in any form for any use, even when it is listed in only one therapeutic category.

USP's decision to classify drugs in multiple categories in some cases but not in others can affect how and whether a formulary meets CMS requirements. A PDP may choose to cover two forms of a particular drug that would enable the formulary to meet CMS standards in a certain class, but disregard the fact that those forms are less commonly prescribed in that class. For instance, a plan that includes Compazine on its formulary presumably gets credit for one of its anti-emetic drugs and one of its anti-psychotics, but this coverage ignores the fact that other anti-emetic drugs may be more important clinically. Furthermore, if a PDP decides to cover two of the least commonly used forms of a particular drug, they might still be fulfilling CMS coverage requirements, but leaving a large gap in coverage for beneficiaries and increasing both switching rates and out-of-pocket (OOP) costs. These considerations are important since the use of a particular drug is not indicated on the prescription. If a plan wishes to draw such distinctions (covering a drug for one use but not another), it must resort to something like prior authorization to enforce its intent.

Clustering of Drugs into Categories. Since drug utilization is heavily concentrated in a few categories and classes in general, formulary decisions for these heavily used drugs will have a disproportionate influence on the overall need for switching from one drug to another or paying out of pocket to continue using an off-formulary drug. The class of renin-angiotensin-aldosterone system inhibitors (one class of the larger category of cardiovascular agents) that is used for hypertension represents 6 percent of all prescription volume, but carries with it the same requirement of two drugs as other classes – such as alpha-adrenergic agents, another class of cardiovascular drugs – that have extremely small prescription volumes. One formulary could fail the statutory test based on alpha-adrenergic agents, while another could pass despite omitting many commonly used renin-angiotensin-aldosterone system inhibitors.

This result may, in fact, be the intent of the CMS and statutory requirements since those obscure drugs are important to the limited number of people who need them. But while the CMS-compliant formularies may do a better job of covering a wide breadth of drugs, they may also force a great number of people using common drugs to switch products. These

issues may require future policy consideration and perhaps modification of USP classification or CMS regulations.